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Title
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Adequacy of risk-reducing gynaecologic surgery in *BRCA1* or *BRCA2* mutation carriers and other women at high risk of pelvic serous cancer

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Abstract The aim of this study was to describe the type of risk-reducing gynaecologic surgery (RRGS) and the extent of pathological evaluation being undertaken for Australasian women at high familial risk of pelvic serous cancer. Surgical and pathology reports were reviewed for women with *BRCA1/BRCA2* mutations, or a family history of breast and ovarian cancer, who underwent RRGS between 1998 and 2008. "Adequate" surgery was defined as complete removal of all ovarian and extra-uterine fallopian tube tissue. "Adequate" pathology was defined as paraffin embedding of all removed ovarian and tubal tissue. Predictors of adequacy were assessed using logistic regression. There were 201 women, including 173 mutation carriers, who underwent RRGS. Of these, 91% had adequate surgery and 23% had adequate pathology. Independent predictors of adequate surgery were surgeon type (OR = 20; 95% CI 2–167; $P = 0.005$ for gynaecologic oncologists versus general gynaecologists), more recent surgery (OR = 1.33/year; 95% CI 1.07–1.67; $P = 0.012$) and younger patient age (OR = 0.93/year of age; 95% CI 0.87–0.99; $P = 0.028$). Independent predictors of adequate pathology were more recent surgery (OR = 1.26/year; 95% CI 1.06–1.49; $P = 0.008$) and surgeon type (OR = 3.1; 95% CI 1.4–6.7; $P = 0.004$ for gynaecologic oncologists versus general gynaecologists). Four serous ovarian cancers and one endometrioid endometrial cancer were detected during surgery or pathological examination. In conclusion Australasian women attending a specialist gynaecologic oncologist for RRGS are most likely to have adequate surgery and pathological examination. Additional education of clinicians and consumers is needed to ensure optimal surgery and pathology in these women.

Keywords *BRCA1/BRCA2* mutations · Cancer prevention · Ovarian cancer · Prophylactic salpingo-oophorectomy · Risk-reducing surgery

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RRGS	Risk-reducing gynaecologic surgery
RRSO	Risk-reducing salpingo-oophorectomy
kConFab	Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
DCIS	Ductal carcinoma in situ
f/up	Follow-up
FDR	First degree relative
BC	Breast cancer
OC	Ovarian cancer
BO	Bilateral oophorectomy
TAH-BSO	Total abdominal hysterectomy and bilateral salpingo-oophorectomy
N/A	Not available
R	Right
L	Left

Introduction

Women carrying a mutation in the breast cancer predisposition genes *BRCA1* or *BRCA2* have a 40–85% cumulative risk of invasive breast cancer to age 70 and a 15–65% cumulative risk of invasive pelvic serous cancer to age 70 [1–5]. The term "pelvic serous cancer" is used because the majority of *BRCA1*- and *BRCA2*-associated gynaecologic cancers appear to originate in the fimbrial end of the fallopian tube rather than the ovary, although they resemble, and have typically been labelled as "serous ovarian cancer" at diagnosis [6]. Women with a family history of breast and "ovarian" cancer, but no identified *BRCA1* or *BRCA2* mutation in the family, are also considered to be at an elevated risk of pelvic serous cancer [7]. This risk increases as the number of "ovarian" cancer cases in the family increases [8].

Risk-reducing salpingo-oophorectomy (RRSO) is the most effective method of reducing pelvic serous cancer risk in women at high familial risk [9–11] and it is the most effective means available of decreasing gynaecologic cancer mortality [12, 13]. In *BRCA1* and *BRCA2* mutation carriers RRSO is estimated to reduce the risk of pelvic serous cancers by 80% and the risk of breast cancer by 50% [14]. Because there is no adequate screening strategy for pelvic serous cancers, RRSO is recommended for women at high familial risk once they have completed child bearing [15–17].

The recommended risk-reducing surgery involves complete resection of the ovaries and fallopian tubes up to their insertion into the cornua of the uterus [15, 17–20] as well as inspection of the peritoneal cavity for macroscopic evidence of malignancy. Removal of the uterus is optional and there have been no reports of malignant transformation in the intramural portion of the fallopian tube when the uterus has not been removed [21, 22]. Peritoneal lavage is not routinely recommended for risk-reducing procedures; however, cytological evaluation of peritoneal washings may increase the chance of detecting malignancy [12, 23, 24].

There is no universal protocol for the pathological evaluation of specimens from RRSO. Sectioning and microscopic examination of both fallopian tubes and ovaries *in toto* by an experienced gynaecological pathologist is recommended [12, 15–18, 20, 25–27]. There is no universal recommendation regarding the number of sections although embedding the ovaries and tubes in their entirety and cutting at least one section from each 2–3 mm paraffin block maximises the detection of occult cancer [16, 25, 27, 28]. In mutation carriers up to 85% of the malignancies detected at RRSO are located in the fallopian tubes, especially in the fimbria, and complete removal and thorough evaluation of these regions is important [25, 29].

Reported rates for occult malignancy of the ovaries and/or fallopian tubes following RRSO range from 0.6 to 18.5%. [9, 10, 18, 24, 26, 27, 29–31] This variability may be due to differences between the studies in terms of sample size, proportion of mutation carriers in the sample, age of included women, extent of pathological evaluation and type of surgery.

We sought to describe the type of surgery and the extent of pathological evaluation performed in Australasian *BRCA1* and *BRCA2* mutation carriers and other women at high familial risk of "ovarian cancer" who undergo risk-reducing gynaecologic surgery (RRGS) and to document the frequency of occult carcinomas.

Patients and methods

Participants were females enrolled in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer (kConFab), a resource of data and biospecimens from multiple-case breast cancer families [32, 33]. Eligibility criteria are available on the website [32]. Families are recruited via 16 Family Cancer Clinics in Australia and New Zealand. At enrolment, blood is drawn for possible future *BRCA* mutation analysis and epidemiology and family history questionnaires are completed. A separately funded and run follow-up study updates cancer events, epidemiological and lifestyle risk factors and uptake of preventative strategies on all female participants every 3 years using a mailed self-administered questionnaire

[34]. Cancer events and surgeries are verified where possible with pathology and surgical reports. All participants provide written informed consent and the study has ethics approval at all recruitment sites.

Women were eligible for the current study if they had: undergone RRGS after enrolment in kConFab, completed at least one round of three-yearly follow-up, a documented deleterious mutation in *BRCA1* or *BRCA2* or a strong family history of breast cancer and at least one case of "ovarian cancer", no personal history of gynaecological cancer and, both an operation report and a pathology report available from their surgery. Women with a personal history of breast cancer, without evidence of distant metastatic disease at the time of RRGS, were included. Non-carriers within a *BRCA1* or *BRCA2* mutation-carrying family were excluded.

Date and type of surgery, type of surgeon and macroscopic findings at surgery were determined from operation reports where possible, or from surgical correspondence and pathology reports. Reason for surgery was determined from self report by the women and from operation reports. Surgeries were performed by the surgeon of the woman's choice at multiple sites throughout Australia and New Zealand and often in institutions not linked with the Family Cancer Centre that the woman had attended. The term "adequate" was used to describe surgical procedures where all ovarian and extra-uterine fallopian tube tissue was completely removed.

For the purposes of this study, we defined surgeon type as follows: general surgeons were registered fellows of the Royal Australasian College of Surgeons; general gynaecologists were registered fellows of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG); gynaecologic oncologists were gynaecologists who also held the Certification or Diploma in Gynaecologic Oncology of the RANZCOG [35].

Details of the pathological evaluation, the presence of occult cancers and the information communicated from surgeon to pathologist were abstracted from pathology reports. The term "adequate" was used to describe pathological examinations where all removed ovarian and tubal tissue was paraffin embedded. In the absence of a universal protocol, we did not define a minimum number of sections to be cut and examined.

New primary gynaecological cancers following RRGS were self-reported and/or reported by enrolled family members in the three-yearly follow-up questionnaire and verified where possible from pathology reports. The duration of follow-up was calculated from the date of RRGS to the date of death or last contact.

Statistical analysis

Differences in the proportion of patients receiving adequate surgery, by surgeon type were tested for using Fisher's Exact Test. Odds ratios and their 95% confidence intervals and associated *P*-values were estimated by logistic regression. All multivariable models included age at RRGS (continuous), year of RRGS (continuous) and surgeon type. Due to lack of evidence of independent association in the final multivariable models we did not include as covariables the type of surgery performed (for the evaluation of adequacy of surgery) and whether or not it was noted in the pathology request form that the sample was from a woman at high risk (for the evaluation of adequacy of pathology). Additional covariates considered for both evaluations were mutation status (mutation carrier versus non-carrier or untested), prior personal history of breast cancer and first degree relatives with ovarian cancer.

All *P*-values were two sided, and those less than 0.05 were considered statistically significant. All statistical analyses were carried out using Stata: Release 10 [36].

Results

From February 1998 to March 2008, 403 women enrolled in kConFab and completing at least one round of follow-up, had undergone RRGS. Of these, 202 were not eligible for the present study (135 had no documented gene mutation and no family history of ovarian cancer; 13 had a personal history of gynaecological cancer; for 18 an operation report was not available; 1 had no available pathology report; 35 were non-carriers within a mutation carrier family). Characteristics of the remaining 201 women are described in Table 1. There were 102 *BRCA1* mutation carriers and 71 *BRCA2* mutation carriers.

Tables 2 and 3 summarise the characteristics of the surgeries and pathological examinations, respectively. Overall 20% of women had both adequate surgery and adequate pathological examination. Adequate surgery was performed in 182 women (91%). The remaining women had neither fallopian tube (10 women) or only one tube (9 women) removed. General gynaecologists and general surgeons performed 18 of the 19 inadequate surgeries. Peritoneal washings were collected in 44 women (22%) and the cytology was abnormal in one woman who was diagnosed with ovarian cancer. Based on the pathology reports, 23% of women had adequate pathological evaluation.

Tables 4 and 5 present a summary of the characteristics of the women by the adequacy of surgery and pathology review, respectively, and the results of univariable and multivariable analyses exploring the associations between them. Multivariable analysis confirmed that the independent predictors of adequate surgery were surgeon type, year of surgery and younger patient age. Gynaecologic oncologists were more likely to perform adequate surgery than

Table 1 Characteristics of the 201 participants

Characteristic	n (%)[a]
Year of RRGS	
Median [range]	2004 [1998–2008]
1998	4
1999	11
2000	13
2001	19
2002	22
2003	24
2004	38
2005	40
2006	16
2007	13
2008	1
Age at time of RRGS (years)	
Median [range]	48 [30–77]
30–39	25 (12)
40–49	93 (46)
50–59	57 (28)
≥60	26 (13)
BRCA mutation status	
BRCA1 mutation carrier	102 (51)
BRCA2 mutation carrier	71 (35)
No documented mutation (includes untested)	28 (14)
Family history of ovarian cancer	
Number of affected first-degree relatives	
0	138 (69)
1	58 (29)
>1	5 (2)
Number of affected second-degree relatives	
0	134 (67)
1	59 (29)
>1	8 (4)
Prior gynaecological surgery (before RRGS)	
None	180 (90)
Unilateral oophorectomy alone	13 (6)
Hysterectomy alone	4 (2)
Unilateral oophorectomy + hysterectomy	4 (2)
Invasive BC diagnosed before RRGS	
Yes	118 (59)
No	83 (41)
Patient reported reason for RRGS	
Cancer prevention	189 (94)
To treat breast cancer[b]	7 (3)
To remove an ovarian/tubal cyst[c]	3 (1)
For cancer[d]	2 (1)

Table 1 continued

Characteristic	n (%)[a]
Time from RRGS to last f/up or death (months)	
Median [range]	35 [0.5–123]

n number, *RRGS* risk-reducing gynaecologic surgery, *DCIS* ductal carcinoma in situ, *f/up* follow-up

[a] Unless otherwise indicated

[b] The surgeon's intention for these seven women was ovarian cancer prevention

[c] The surgeon's intention for these three women was ovarian cancer prevention

[d] These two women had cancer detected at RRGS. The surgeon's intention for each was cancer prevention

Table 2 Characteristics of Surgery

Characteristic	n (%)
Type of surgery	
Laparoscopic	138 (69)
Abdominal	53 (26)
Conversion (laparoscopic > abdominal)	10 (5)
Hysterectomy at time of RRGS	93 (46)
Surgeon type	
Gynaecologic oncologist	105 (52)
General gynaecologist	85 (42)
General surgeon	11 (5)
Adequacy of surgery	
Adequate	182 (91)
Not adequate[a]	19 (9)
Macroscopic abnormality noted at surgery	
Yes	5 (2)
Not reported	196 (98)
Peritoneal lavage	
Yes	44 (22)
Not reported	157 (78)

n number, *RRGS* risk-reducing gynaecologic surgery

[a] Nine women had only one tube removed and 10 women had neither tube removed

general gynaecologists (OR = 20; 95% CI 2,167; P = 0.005) and general surgeons (OR = 89; 95% CI 8,1031; P < 0.001). Regardless of surgeon type, more recent surgery was also more likely to be adequate (OR = 1.33 per year; 95% CI 1.07,1.67; P = 0.012). Only 3 of the 19 inadequate surgeries were performed after 2004. The independent predictors of adequate pathological examination were more recent surgery (OR = 1.26; 95% CI 1.06,1.49; P = 0.008) and surgeon type. Surgeries

Table 3 Characteristics of pathology

Characteristic	n (%)
Clinical notes indicated high risk	
Yes	151 (75)
No	37 (18)
Missing	13 (6)
Adequacy of pathological examination	
Adequate	46 (23)
Not adequate	155 (77)
Extent of ovarian examination	
Adequate (all tissue embedded)	65 (32)
Not adequate[a]	136 (68)
Extent of tubal examination[b]	
Adequate (all tissue embedded)	42 (22)
Not adequate[a]	149 (78)
Fimbria specifically examined[b]	
Yes	28 (15)
Not reported	163 (85)
Peritoneal washings cytology (n = 44)	
Normal	43 (98)
Cancer	1 (2)
Occult cancer	
"Ovarian"	4 (2)
Endometrial	1 (0.5)

n number

[a] Only sections of tissue embedded or no documentation of what was embedded

[b] n = 191 because 10 women had no fallopian tubes removed

performed by gynaecologic oncologists were more likely to be associated with adequate pathology than surgeries performed by general gynaecologists (OR = 3.12; 95% CI 1.4,6.7; P = 0.004).

All women who had a hysterectomy had adequate surgery. There was no difference between abdominal or laparoscopic surgery in terms of adequacy. Clinical notes provided by the surgeon on the pathology request form, were included in 188 pathology reports. Of these 80% documented the woman's elevated risk for "ovarian" cancer. There was no significant difference between the three surgeon types in documenting the high risk status. Although documenting high risk status predicted for adequate pathology in the univariable analysis it was not an independent predictor of adequate pathology.

Four (2%) pelvic serous cancers were detected at surgery (Table 6). All were in mutation carriers and all were reported as ovarian in origin although there was little detail in any about the degree of pathological scrutiny of the fallopian tubes. Tubal carcinoma in situ was not reported in any of the 201 cases. The youngest age at cancer diagnosis was 40 years in a *BRCA1* mutation carrier. One endometrioid adenocarcinoma of the uterus was diagnosed in a woman with no documented genetic mutation but a past history of breast cancer and tamoxifen-related postmenopausal bleeding.

During the follow-up period (median 35 months) one peritoneal adenocarcinoma was reported in a 70-year-old *BRCA1* mutation carrier, 8 years after RRGS. She had undergone adequate surgery but inadequate pathological examination. Six deaths were reported during follow-up and all were attributed to metastatic breast cancer.

Discussion

This prospective study of RRGS in Australasian women at high familial and genetic risk for pelvic serous cancer has revealed the majority had adequate surgery, the minority had adequate pathological evaluation, and the detection rate for occult cancers (2%) was relatively low. Because many pelvic serous cancers in mutation carriers are believed to originate in the tubal fimbria [6,] it is particularly concerning that 9% of operations left extra-uterine fallopian tubes in situ. As expected, more recent year of surgery was associated with more adequate surgery and pathology reflecting improved knowledge of the surgeons and pathologists over time.

Surgery performed by a specialised gynaecologic oncologist was more likely to be adequate. This may reflect greater awareness of the high cancer risk for these women and the importance of complete removal of both ovaries and tubes. Surgeries performed by gynaecologic oncologists were also more likely to be associated with adequate pathology, possibly because gynaecologic oncologists are more likely to practice within large teaching hospitals with academic pathology departments performing better quality examinations.

Only 23% of pathology reports documented that ovarian and tubal tissues were embedded *in toto*. Ensuring all tissue is embedded maximises the ability to detect microscopic occult cancers and, because only the embedded tissue is saved, it allows repeat examination of tissues at a later date if required. Our result compares poorly with others in the literature. In one recent multi-institutional study of RRSO in *BRCA1/2* mutation carriers, pathology reports from 385 women were centrally reviewed and 59% documented embedding and examining the ovaries and fallopian tubes *in toto* [37]. Two other smaller series reported full sectioning of the ovaries and fallopian tubes in 74% [24] and 33% of women, respectively [18]. In the former series all cases with full sectioning had surgery performed at one specialised institution while none of the cases where surgery was performed by outside institutions had full sectioning performed [24]. The fact that surgical procedures in

Table 4 Predictors of adequate surgery

Characteristic	Adequacy of surgery n (%)		Univariable analysis	Multivariable analysis[a]
	Yes	No	Odds ratio (95% CI), P value	Odds ratio (95% CI), P value
Age at RRGS (years)				
30–39	24 (96)	1 (4)	1.95 (0.23–16.7), 0.5	2.09 (0.22–20.0), 0.5
40–49	86 (92)	7 (8)	1.00	1.00
50–59	49 (86)	8 (14)	0.50 (0.17–1.46), 0.2	0.55 (0.17–1.84), 0.3
≥60	23 (90)	3 (10)	0.62 (0.15–2.60), 0.5	0.75 (0.14–3.93), 0.7
Trend (per year)			0.94 (0.89–0.99), 0.01	0.93 (0.87–0.99), 0.028
Year of RRGS				
1998–2001	39 (83)	8 (17)	0.43 (0.16–1.16), 0.1	0.49 (0.16–1.55), 0.2
2002–2005	114 (92)	10 (8)	1.00	1.00
2006–2008	29 (97)	1 (3)	2.54 (0.31–20.7), 0.4	4.22 (0.46–38.7), 0.2
Trend (per year)			1.33 (1.08–1.64), 0.007	1.33 (1.07–1.67), 0.012
Type of surgeon				
Gynaecologic oncologist	104 (98)	1 (2)	1.00	1.00
General Gynaecologist	71 (85)	14 (15)	0.05 (0.006-0.38), 0.004	0.05 (0.006-0.40), 0.005
General Surgeon	7 (64)	4 (36)	0.02 (0.002–0.17), 0.001	0.01 (0.001–0.13), <0.001
Type of Surgery				
Abdominal[b]	58 (92)	5 (8)	1.00	1.00
Laparoscopic	124 (90)	14 (10)	0.76 (0.26–2.22), 0.6	0.89 (0.26–3.06), 0.8
BRCA1/2 carrier				
No/untested	24 (88)	4 (12)	1.00	1.00
Yes	158 (91)	15 (9)	1.76 (0.54–5.73), 0.4	1.72 (0.42–7.09), 0.5
Prior invasive BC				
No	79 (96)	4 (4)	1.00	1.00
Yes	103 (87)	15 (13)	0.18 (0.04–0.78), 0.02	0.24 (0.05–1.24), 0.09
≥1 FDR with OC				
No	125 (91)	13 (9)	1.00	1.00
Yes	57 (90)	6 (10)	0.99 (0.36–2.73), 0.9	1.61 (0.48–5.40), 0.4

RRGS risk-reducing gynaecological surgery, *FDR* first degree relative, *BC* breast cancer, *OC* ovarian cancer

[a] Adjusted for age (continuous), year of surgery (continuous) and type of surgeon (categorical), as appropriate

[b] Includes conversion from laparoscopic to abdominal

our study were performed at numerous centres across Australia and New Zealand, each with a different pathology laboratory, may have contributed to our result.

Four serous ovarian cancers, one endometrioid endometrial cancer and no fallopian tube cancers were diagnosed at RRGS. Three of the serous ovarian cancers were in *BRCA1* mutation carriers. This is consistent with the literature where the majority of reported occult carcinomas arise in *BRCA1* mutation carriers [18, 29, 38]. Our "occult cancer" rate of 2% was at the lower end of the reported range (0.6–18.5%) [9, 10, 18, 24, 26, 27, 29–31] but was comparable to the 2.5% rate recently reported in a review of 647 mutation carriers [37] and to the 0.6% rate from another review of 175 mutation carriers [31]. Our apparent low cancer rate may be a result of the majority of patients having inadequate pathological examinations. Cancer

detection rates of 1–3% are reported for confirmed mutation carriers in series without documentation of pathological technique [10, 39], but much higher rates of 10–26% are reported when thorough pathological examination with serial sectioning is mandated [16, 40]. For example, in one series of 67 BRCA1/2 mutation carriers undergoing RRGS, a protocol of complete removal and 2 mm serial sectioning of both ovaries and fallopian tubes was the strongest predictor of occult cancer detection, and was more important than age and mutation type [16].

Most pathology reports in this study did not document the number of sections taken from each ovary and tube. Pathology reports should be improved to include details of how the tissue was processed and examined so that physicians caring for high risk women can be assured that the tissue has been thoroughly examined. We believe a

Table 5 Predictors of adequate pathology

Characteristic	Adequacy of pathology n (%)		Univariable analysis	Multivariable analysis[a]
	Yes	No	Odds ratio (95% CI), P value	Odds ratio (95% CI), P value
Age at RRGS (years)				
30–39	2 (12)	23 (88)	0.18 (0.04–0.83), 0.03	0.21 (0.05–0.99), 0.05
40–49	30 (29)	63 (71)	1.00	1.00
50–59	11 (19)	46 (81)	0.50 (0.23–1.10), 0.09	0.52 (0.23–1.18), 0.1
≥60	3 (13)	23 (87)	0.27 (0.08–0.98), 0.05	0.27 (0.07–1.03), 0.06
Trend (per year)			0.98 (0.94–1.02), 0.3	0.98 (0.94–1.02), 0.4
Year of RRGS				
1998–2001	8 (15)	39 (85)	0.90 (0.37–2.18), 0.8	1.03 (0.41–2.58), 0.9
2002–2005	23 (18)	101 (82)	1.00	1.00
2006–2008	15 (50)	15 (50)	4.39 (1.88–10.2), 0.001	6.06 (2.38–15.4), <0.001
Trend (per year)			1.24 (1.06–1.45), 0.009	1.26 (1.06–1.49), 0.008
High risk on request form				
No	6 (12)	31 (88)	1.00	1.00
Yes	40 (27)	111 (73)	1.86 (0.72–4.79), 0.2	1.60 (0.59–4.34), 0.4
Unknown	0 (0)	13 (100)	–	–
Type of surgeon				
Gynaecologic oncologist	33 (31)	72 (69)	1.00	1.00
General gynaecologist	11 (12)	74 (88)	0.32 (0.15–0.69), 0.003	0.32 (0.15–0.70), 0.004
General surgeon	2 (18)	9 (82)	0.48 (0.10–2.37), 0.4	0.48 (0.10–2.41), 0.4
BRCA1/2 carrier				
No/untested	10 (30)	18 (70)	1.00	1.00
Yes	36 (20)	137 (80)	0.47 (0.20–1.11), 0.09	0.49 (0.20–1.23), 0.1
Prior invasive BC				
No	21 (25)	62 (75)	1.00	1.00
Yes	25 (20)	93 (80)	0.72 (0.37–1.40), 0.3	0.92 (0.44–1.90), 0.8
≥1 FDR with OC				
No	30 (21)	108 (79)	1.00	1.00
Yes	16 (24)	47 (76)	1.23 (0.61–2.46), 0.6	1.53 (0.72–3.22), 0.3

RRGS risk-reducing gynaecologic surgery, *BC* breast cancer, *FDR* first degree relative, *OC* ovarian cancer

[a] Adjusted for age (continuous), year of surgery (continuous) and type of surgeon (categorical), as appropriate

standardised tissue processing and reporting protocol is required to ensure all women have the same extent of pathological examination and to ensure early stage malignancies are not missed. Many "ovarian cancers" in mutation carriers are now thought to originate in the tubal fimbriae [41, 42] and pathologists must be made aware of this to ensure the tubes and fimbria are fully embedded and thoroughly sectioned and examined.

Although communication of high cancer risk from surgeon to pathologist was not an independent predictor of adequate pathology, educating surgeons to include this information on the pathology request form is still important. Ovaries and fallopian tubes removed for reasons other than cancer risk reduction do not require the same extent of pathological evaluation. Without appropriate communication from the surgeon it is difficult for pathologists to determine the specimens needing to be fully embedded and thoroughly examined. It may also be helpful for surgeons to request all tissue be embedded.

Despite our concern that microscopic cancers were missed due to inadequate pathology, only one cancer was diagnosed during follow up. This is consistent with the rates of 1–3% reported in the literature following RRSO. [10, 16, 31, 39] One explanation for this is that any cancers not detected were of early stage and the risk-reducing surgery alone was curative. If true, it could be argued that complete pathological evaluation of removed tissues is of academic interest only and is unlikely to change patient outcomes. Alternatively, our follow-up time may be too short for cancers to manifest. There is insufficient information on the long term clinical consequences of early pelvic serous cancers and further research is required.

Table 6 Characteristics of cancers found in RRGS specimens

Age	Mutation	Surgery	Pathology examination	Pathology findings
63	BRCA1	BSO + R iliac node dissection	Ovaries—fully embedded/sectioned	Serous "ovarian" carcinoma
			Tubes—no details of amount embedded or examined	Tumour involving ovaries and common iliac nodes. Normal tubes.
				Stage IIIC (T2b N1 M0)
40	BRCA1	TAH-BSO + omentectomy + peritoneal washings	Ovaries and tubes—no details of amount embedded or examined	Serous "ovarian" carcinoma
				Tumour involving ovaries, uterine serosa, pelvic side wall and sigmoid colon. Normal tubes. Peritoneal washings positive for adenocarcinoma.
				At least Stage IIC (T2c Nx M0)
49	BRCA1	TAH-BSO + partial omentectomy	Ovaries and tubes—no details of amount embedded or examined	Serous "ovarian" carcinoma
				Tumour involving ovaries, normal tubes.
				At least stage IC (T1c Nx M0)
55	BRCA2	BO[a]	Representative sections of both ovaries embedded and sectioned	Serous "ovarian" carcinoma
				Extensive infiltration of L ovary by poorly differentiated carcinoma. R ovary normal.
				Stage IA (T1a N0 M0)
55	Not detected	TAH-BSO	Ovaries and tubes—no details of amount embedded or examined	Grade 1 endometrioid endometrial carcinoma
				At least stage IA (T1a Nx M0)

RRGS risk-reducing gynaecological surgery, *BO* bilateral oophorectomy, *TAH-BSO* total abdominal hysterectomy and bilateral salpingo-oophorectomy, *N/A* not available, *R* right, *L* = left

[a] This patient proceeded to a second surgery 2 weeks later where the uterus, fallopian tubes and omentum were removed and peritoneal washings were taken. There was no further carcinoma detected

Thorough pathological evaluation of removed tissue will be important to gather information to enable such research. Women in whom early cancers are detected should be given the options of additional surgical staging, chemotherapy and closer follow-up. Important preventative and therapeutic implications for the future could result from detecting and studying these early cancers.

This study was multi-institutional and thus is likely a true reflection of the management of high risk women in Australia and New Zealand. However, the study has some limitations. We relied on the information detailed in operation and pathology reports to determine the adequacy of surgery and pathology. If the operation report did not describe the procedure in sufficient detail to determine what tissues were removed, we assumed that the tissue received by the pathologist represented the tissue removed by the surgeon. If tissue was removed but not submitted for pathology review we may have underestimated the number of adequate surgeries. We also assumed that ovarian and tubal tissue was not fully embedded if the pathology report did not specifically document this. It is possible that some specimens were embedded *in toto* but not reported as such. This assumption may have led to an underestimation of the rate of adequate pathological examinations. However, our assumption that tissue that was all embedded was also thoroughly sectioned and examined may have caused us to overestimate the proportion of specimens adequately examined.

Australasian *BRCA1* and *BRCA2* mutation carriers and women at high familial risk of "ovarian" cancer who elect RRSO must receive high quality care that will reduce their risk of gynaecological cancer. This study highlights the need for standardised surgical techniques and tissue processing protocols for RRSO. Clinicians who discuss RRSO with these women should consider referring them to specialist gynaecologic oncologists for their surgery, or at least should discuss the specifics of optimal surgery and pathology with the woman's existing gynaecologist or general surgeon if he/she is planning to undertake the surgery. High risk women themselves should be educated about the likely pathogenesis of pelvic serous cancers from the fallopian tubes rather than the ovaries and hence the type of surgery that is optimal. Using the term "ovarian cancer" to describe this disease is misleading and arguably should be abandoned to reflect the emerging evidence regarding the pathogenesis of this disease.

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Conflict of interests None declared.

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